SUBCLINICAL SIGNS IN LRRK2 MUTATION CARRIERS

K.K. Johansen1,2, L.R. White1,2, S.N. Kvam1,2, M. Farrer3, J.O. Aasly1,2

1St Olavs University Hospital, 2Norwegian University of Science and Technology, Trondheim, Norway, 3University of British Columbia, Vancouver, BC, Canada

Introduction: Several non-motor features have been reported to precede the motor signs of Parkinson's disease (PD) by several years. However, the time of onset of non-motor and motor symptoms is still debated. Healthy individuals carrying a PD-related mutation are candidates for studying the earliest disease signs.

Aims: A blinded investigation of healthy family members of LRRK2-PD patients for clinical differences between mutation carriers and non-carriers.

Methods: A total of 47 family members of LRRK2-PD patients were included in the present study and were screened for the p.G2019S and p.N1437H substitutions in the LRRK2 gene. A standardized case report form was filled out in each case, including general medical evaluation, neurological examination with UPDRS, an olfaction test, mood, sleep and cognitive questionnaires.

Results: Thirty-two study participants were positive, and 15 were negative for a LRRK2 mutation. Higher UPDRS motor scores, more frequent reports of urinary problems, and fewer hours of sleep were found in mutation carriers compared to non-carriers. The mutation carriers with UPDRS ≥ 8 were all aged over 50 years, had shorter overall sleeping hours, more frequent urinary and constipation problems, higher mood scores and body mass index. Deterioration of olfaction was not detected in either group.

Conclusion: Healthy LRRK2 mutation carriers presented subclinical parkinsonian motor and non-motor signs in the apparent absence of olfactory loss. Longitudinal studies will determine whether these changes precede alterations detectable by neuroimaging.